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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,186	10/19/2000	Tan Thanh Dinh	ECV-5611	9184

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EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	**PAPER NUMBER**
1743	14

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/693,186	Applicant(s) DINH ET AL.
	Examiner Maureen M. Wallenhorst	Art Unit 1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) *1-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-19,21 and 22* is/are rejected.

7)☒ Claim(s) *9 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-6 and 12-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Korte et al. (submitted in the Information Disclosure Statement filed on June 22, 2001).

Korte et al teach of a method for one-dimensional thin layer chromatography to separate phospholipids. In the method, a mixture of phospholipids such as phosphatidylcholine, phosphatidylethanolamine and phosphatidylinositol are extracted into a 2:1 extraction solvent of chloroform and methanol. The extraction solvent containing the phospholipids is then spotted onto a silica TLC plate, and placed into an elution solvent mixture. The TLC plate is developed in one direction, which allows for the separation of the phospholipids. The separated phospholipids are then visualized and detected. See pages 48-49 in Korte et al.

4. Claims 1-6 and 12-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Entezami et al. (submitted in the Information Disclosure Statement filed June 22, 2001).

Entezami et al teach of a method for the analysis and separation of phospholipids by thin layer chromatography (TLC). In the method, a mixture of standard phospholipids such as sphingomyelin, phosphatidylcholine, phosphatidylethanolamine, etc are extracted into a volume of 2:1 chloroform and methanol. Spots of the extraction solvent containing the phospholipids are applied to a silica TLC plate, and then the plates are chromatographed in one direction in a TLC tank containing an elution solvent. Following development of the chromatogram, the individual phospholipids are scanned and detected. See pages 325-326 of Entezami et al.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 7-8 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Korte et al or Entezami et al in view of Schmitz et al (submitted in the Information Disclosure Statement filed on June 22, 2001). For a teaching of Korte et al and Entezami et al, see previous paragraphs in this Office action. Korte et al and Entezami et al fail to teach that the

elution solvent in the method for performing TLC contains chloroform, methanol, acetic acid and an aqueous solution of potassium chloride.

Schmitz et al teach of a method for the one-dimensional separation of phospholipids by thin layer chromatography (TLC). A mixture of phospholipids such as sphingomyelin, phosphatidylcholine and phosphatidylethanolamine are applied to a TLC plate, and separated in a one-step procedure using an elution solvent containing acetic acid, chloroform, methanol and potassium chloride in distilled water. See page 67 of Schmitz et al.

Based upon a combination of either Korte et al or Entezami et al with Schmitz et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the elution solvent containing chloroform, methanol, acetic acid and potassium chloride taught by Schmitz et al as the elution solvent in the TLC methods disclosed by Korte et al and Entezami et al since Schmitz et al teach that such an elution solvent in a TLC method serves to effectively separate several different types of phospholipids, which is the purpose of the methods taught by the primary references to Korte et al and Entezami et al., and is equivalent in function to the elution solvents disclosed in these primary references.

8. Claims 10-11 and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Korte et al or Entezami et al in view of White et al (WO 99/50655). For a teaching of Korte et al and Entezami et al, see previous paragraphs in this Office action. Korte et al and Entezami et al fail to teach that the separated phospholipids are detected in an ultraviolet detection system after staining with primulin.

White et al teach of a method for separating target molecules such as an individual phospholipid from a mixture of phospholipids, that employs thin layer chromatography (TLC).

In one embodiment of the method, phosphatidylinositol is separated from a mixture containing the phosphatidylinositol and phosphatidylcholine by first extracting the phospholipids into an extraction solvent containing methanol and chloroform. Spots of the extraction solvent containing the phospholipids are then applied to a TLC silica plate. One-dimensional thin layer chromatography is then performed by the elution of a solvent in one direction. The separated phospholipid can then be detected by staining the phospholipid with primulin and exposing it to ultraviolet light. See claims 8-10 and 26 in White et al.

Based upon a combination of either Korte et al or Entezami et al with White et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to detect the separated phospholipids in the methods taught by Korte et al and Entezami et al by staining the separated phospholipids with primulin followed by exposure to ultraviolet light since White et al teach that this is one known way in which to detect and quantitate separated phospholipids, that is equivalent in function to the means for detection disclosed by Korte et al and Entezami et al.

9. Claims 9 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims since none of the prior art of record teaches or fairly suggests a method for separating phospholipids by one-dimensional thin layer chromatography, wherein the elution solvent in the method consists essentially of 35 parts chloroform, 10 parts methanol, 9.8 parts acetic acid and 1.2 parts of an aqueous solution of potassium chloride.

10. Applicant's arguments filed May 23, 2003 have been fully considered but they are not persuasive.

Applicants argue the rejection of the claims under 35 USC 102 (b) as being anticipated by the references to Korte et al and Entezami et al by stating that the separation of the phospholipids in the methods taught by these references is not sufficient to separately quantify the individual phospholipids in the mixtures, as recited in the instant claims, since the chromatograms of the separated phospholipids in each reference depict overlapping peaks. For example, in Korte, Applicants argue that the peak for PS in Figure 3 overlaps with the peak for PI, and therefore, the peak for PS actually represents a mixture of phospholipid species. In response to this argument, it is not understood how Applicant can state that the peaks depicted in the chromatograms of Korte and Entezami overlap since separate peaks for each phospholipid are depicted, and the area under each of these separate peaks can be quantitated, thus making each phospholipid separately quantifiable, as in the instant invention. The peaks for each phospholipid on the chromatograms are next to one another, but do not overlap. If these peaks did overlap, the peaks would be drawn on top of one another. In a similar fashion, the peaks depicted in Figure 2 of the instant application are located next to one another, and some of the peaks have the same heights as one another. It is not understood how Applicants can assert that the PS spot in Figure 3 of Korte actually contains a mixture of PS and PI when the reference contains no factual evidence of this. Applicants argue that a spot on the TLC plate must contain a single phospholipid species to be separately quantifiable as in the instant invention. In response to this argument, it is noted that each separate spot on the TLC plates taught by Korte and Entezami is depicted and taught as containing only one phospholipid. Otherwise, the individual peaks in the chromatograms would not be labeled with only one phospholipid. Only one peak is depicted for each individual separated phospholipid spot on the TLC plate, and each

peak is only attributed to one phospholipid, indicating that the phospholipid is separately quantifiable.

Applicants argue the rejection of the claims under 35 USC 103 using the combination of either Korte or Entezami with Schmitz by stating that Schmitz teaches away from the instant invention since Schmitz teaches that the use of an elution solvent containing chloroform, methanol, acetic acid and potassium chloride results in overlapping TLC spots when phospholipid mixtures in the presence of neutral lipids are separated using thin layer chromatography. Applicants argue that since the instant invention and the methods of both Korte and Entezami teach the separation of a phospholipid mixture containing neutral lipids therein, one of ordinary skill in the art would not be motivated to use the elution solvent of Schmitz in the methods of the instant invention, Korte or Entezami. In response to this argument, it is noted that Schmitz does not attribute the elution solvent to the problem of overlapping TLC spots in phospholipid mixtures containing neutral lipids therein. Therefore, it cannot be concluded that the elution solvent taught by Schmitz causes the overlapping TLC spots, and would not be efficient in separating phospholipids containing neutral lipids therein. On the contrary, this solvent must not cause overlapping TLC spots since it is used in the instant invention, and Applicants claim that non-overlapping spots are achieved in the separation of mixtures of phospholipids containing neutral lipids therein. One of ordinary skill in the art would be motivated to use the elution solvent taught by Schmitz in the methods taught by Korte and Entezami since the elution solvent is not attributed to the problem of overlapping TLC spots, and Schmitz teaches of excellent separation of phospholipids obtained by using the elution solvent.

Applicants argue the rejection of the claims under 35 USC 103 as being obvious over the combination of either Korte or Entezami with White by stating that Korte and Entezami do not teach of separating phospholipids to obtain discrete, detectable spots that are separately quantifiable, and that White fails to teach the use of a single TLC migration to separate phospholipids. Applicants' argument with respect to Korte and Entezami has been addressed in previous paragraphs. In response to Applicants' argument concerning White, it is noted that the primary references to Korte and Entezami teach of the use of a single TLC migration to separate a mixture of phospholipids. The secondary reference to White is used to show the obviousness of using a detection method involving staining with primulin followed by exposure to ultraviolet light to detect the separated phospholipids on the TLC plates taught by Korte and Entezami since White discloses this to be a known and conventional way in which to detect and quantitate separated phospholipids, that is equivalent in function to the means for detection disclosed by Korte and Entezami.

For all of the above reasons, Applicants' arguments are not found persuasive.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 703-308-3912. The examiner can normally be reached on Monday-Wednesday from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0661.

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

June 2, 2003

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
PRIMARY EXAMINER
GROUP [redacted] 1700